

CLAIMS

1. A flexible hyperbranched dendron polymer comprising:
a surface defined by the polymer;
a polyethyleneimine core within the surface;
5 a plurality of primary amine groups at the surface; and
a plurality of secondary and tertiary amine groups positioned at the core.
2. The polymer of claim 1, wherein the polymer has a molecular weight of greater than or
equal to about 10 kD.
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3. The polymer of claim 2, wherein the polymer has a molecular weight of less than or
equal to about 25 kD.
4. The polymer of claim 3, wherein the polymer has a secondary to tertiary amine ratio of
15 less than or equal to about 1.5 to 1.
5. The polymer of claim 4, wherein the polymer has a secondary to tertiary amine ratio of
less than or equal to about 1.3 to 1.
- 20 6. The polymer of claim 4, wherein the polymer has a secondary to tertiary amine ration of
greater than about 1.0 to 1.
7. The polymer of claim 4, wherein the polymer has a secondary to tertiary amine ration of
greater than or equal to about 1.2 to 1.
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8. The polymer of claim 1, wherein the polymer is made by a process comprising iterative
attachment of ethyleneimine moieties to a branched polyethyleneimine core.
9. The polymer of claim 8, wherein the process increases the amount of secondary and
30 tertiary amines in the polymer while maintaining a plurality of primary amines on the surface of
the polymer.

10. The polymer of claim 8, wherein the process comprising iterative attachment of ethyleneimine moieties to a branched polyethyleneimine core comprises:

- (a) reacting polyethyleneimine with chloroethyl amine;
- (b) reacting the modified polyethyleneimine of step (a) with chloroethyl amine; and
- (c) reacting the modified polyethyleneimine of step (b) with chloroethyl amine.

11. A hyperbranched dendron polymer having a randomly branched structure, a molecular weight of about 10 to 25 kD, and a ratio of secondary to tertiary amine groups of less than or equal to about 1.5 to 1.

12. The polymer of claim 11, wherein the ratio of secondary to tertiary amine groups is less than or equal to about 1.3 to 1.

13. The polymer of claim 12, wherein the ratio of secondary to tertiary amine groups is greater than or equal to about 1.2 to 1.

14. The polymer of claim 12, wherein the molecular weight is greater than or equal to about 12 kD.

15. The polymer of claim 12, wherein the molecular weight is less than or equal to about 15 kD.

16. The polymer of claim 11, wherein the polymer comprises:
a surface defined by the polymer;
a polyethyleneimine core within the surface;
a plurality of primary amine groups at the surface; and
a plurality of secondary and tertiary amine groups positioned at the core.

17. The polymer of claim 11, wherein the polymer is made by a process comprising iterative attachment of ethyleneimine moieties to a branched polyethyleneimine core.

18. The polymer of claim 17, wherein the process increases the amount of secondary and tertiary amines in the polymer while maintaining a plurality of primary amines on a surface of the polymer.

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19. The polymer of claim 18, wherein the process comprising iterative attachment of ethyleneimine moieties to a branched polyethyleneimine core comprises:

- (a) reacting polyethyleneimine with chloroethyl amine;
- (b) reacting the modified polyethyleneimine of step (a) with chloroethyl amine; and
- (c) reacting the modified polyethyleneimine of step (b) with chloroethyl amine.

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20. A hyperbranched dendron polymer made by a process comprising iterative attachment of ethyleneimine moieties to a branched polyethyleneimine core, wherein the process increases the amount of secondary and tertiary amines in the polymer while maintaining a plurality of primary amines on a surface of the polymer.

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21. The polymer of claim 20, wherein the process comprising iterative attachment of ethyleneimine moieties to a branched polyethyleneimine core comprises:

- (a) reacting polyethyleneimine with chloroethyl amine;
- (b) reacting the modified polyethyleneimine of step (a) with chloroethyl amine; and
- (c) reacting the modified polyethyleneimine of step (b) with chloroethyl amine.

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22. The polymer of claim 20, wherein the polymer has a molecular weight of greater than or equal to about 10 kD.

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23. The polymer of claim 22, wherein the polymer has a molecular weight of less than or equal to about 25 kD.

24. The polymer of claim 23, wherein the polymer has a secondary to tertiary amine ratio of less than or equal to about 1.5 to 1.

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25. The polymer of claim 24, wherein the polymer has a secondary to tertiary amine ratio of less than or equal to about 1.3 to 1.

26. The polymer of claim 24, wherein the polymer has a secondary to tertiary amine ration of greater than about 1.0 to 1.

27. The polymer of claim 24, wherein the polymer has a secondary to tertiary amine ration of greater than or equal to about 1.2 to 1.

28. A complex between a hyperbranched dendron polymer and a nucleic acid molecule comprising:

a nucleic acid molecule; and

a hyperbranched dendron polymer selected from at least one of the group consisting of

(a) a flexible hyperbranched dendron polymer comprising: a surface defined by the polymer, a polyethyleneimine core within the surface, a plurality of primary amine groups at the surface, and a plurality of secondary and tertiary amine groups positioned at the core.;

(b) a hyperbranched dendron polymer having a randomly branched structure, a molecular weight of about 10 to 25 kD, and a ratio of secondary to tertiary amine groups of less than or equal to about 1.5 to 1; and

(c) hyperbranched dendron polymer made by a process comprising iterative attachment of ethyleneimine moieties to a branched polyethyleneimine core, wherein the process increases the amount of secondary and tertiary amines in the polymer while maintaining a plurality of primary amines on a surface of the polymer.

29. The complex of claim 28, wherein the hyperbranched dendron polymer has a ratio of secondary to tertiary amine groups is less than or equal to about 1.3 to 1.

30. The complex of claim 29, wherein the hyperbranched dendron polymer has a ratio of secondary to tertiary amine groups is greater than or equal to about 1.2 to 1.

31. The complex of claim 29, wherein the hyperbranched dendron polymer has a molecular weight is greater than or equal to about 12 kD.
- 5 32. The complex of claim 29, wherein the hyperbranched dendron polymer has a molecular weight is less than or equal to about 15 kD.
33. The complex of claim 28, wherein the hyperbranched dendron polymer comprises:
a surface defined by the polymer;
10 a polyethyleneimine core within the surface;
a plurality of primary amine groups at the surface; and
a plurality of secondary and tertiary amine groups positioned at the core.
34. The complex of claim 28, wherein the hyperbranched dendron polymer is made by a
15 process comprising:
(a) reacting polyethyleneimine with chloroethyl amine;
(b) reacting the modified polyethyleneimine of step (a) with chloroethyl amine; and
(c) reacting the modified polyethyleneimine of step (b) with chloroethyl amine.
- 20 35. The complex of claim 28, wherein the complex is stable in the presence of serum.
36. The complex of claim 28, wherein the nucleic acid comprises DNA.
37. The complex of claim 36, wherein the complex has a size of less than or equal to 100
25 nanometers.
38. The complex of claim 36, wherein the DNA encodes at least a therapeutic gene.
39. The complex of claim 38, wherein the complex results in an optimum cell transfection
30 efficiency at low N/P ratios.

40. The complex of claim 38, wherein the complex results in an optimum cell transfection efficiency at N/P ratios less than or equal to about 10.

41. The complex of claim 38, wherein the complex results in an optimum cell transfection efficiency at N/P ratios between about 6 and 9.

42. The complex of claim 38, wherein introduction of the complex to the body of a mammal results in prolonged expression of the therapeutic gene which extends more than 72 hours after introduction of the complex.

43. The complex of claim 38, wherein introduction of the complex to the body of a mammal results in prolonged expression of the therapeutic gene which extends for eight days after introduction of the complex.

44. The complex of claim 38, wherein introduction of the complex to the body of a mammal results in transfection of cells by the complex and expression of the therapeutic gene in organs located at a distance from a site at which the complex was introduced.

45. The complex of claim 44, wherein the therapeutic gene is expressed in a lymph node of the mammal.

46. The complex of claim 28, wherein the complex has diameter of less than or equal to about 100 nm.

47. The complex of claim 46, wherein the complex has a diameter of between about 50 and 100 nm.

48. The complex of claim 46, wherein the complex has a diameter of between about 50 and 70 nm.

49. The complex of claim 28, wherein the nucleic acid molecule comprises siRNA.

50. A method of transferring a nucleic acid into cells comprising administering to said cells a complex according to claim 28.

5 51. The method of claim 50, wherein the hyperbranched dendron polymer has a ratio of secondary to tertiary amine groups is less than or equal to about 1.3 to 1.

52. The method of claim 51, wherein the hyperbranched dendron polymer has a ratio of secondary to tertiary amine groups is greater than or equal to about 1.2 to 1.

10 53. The method of claim 50, wherein the hyperbranched dendron polymer has a molecular weight is greater than or equal to about 12 kD.

15 54. The method of claim 53, wherein the hyperbranched dendron polymer has a molecular weight is less than or equal to about 15 kD.

55. The method of claim 50, wherein the hyperbranched dendron polymer comprises:
a surface defined by the polymer;
a polyethyleneimine core within the surface;
20 a plurality of primary amine groups at the surface; and
a plurality of secondary and tertiary amine groups positioned at the core.

56. The method of claim 50, wherein the hyperbranched dendron polymer is made by a process comprising:

- 25 (a) reacting polyethyleneimine with chloroethyl amine;
(b) reacting the modified polyethyleneimine of step (a) with chloroethyl amine; and
(c) reacting the modified polyethyleneimine of step (b) with chloroethyl amine.

57. The method of claim 50, wherein the complex is stable in the presence of serum.

30 58. The method of claim 50, wherein the nucleic acid comprises DNA.

59. The method of claim 58, wherein the complex has a size of less than or equal to 100 nanometers.
- 5 60. The method of claim 58, wherein the DNA encodes at least a therapeutic gene.
61. The method of claim 58, wherein optimum cell transfection efficiency is achieved at low N/P ratios.
- 10 62. The method of claim 61, wherein optimum cell transfection efficiency is achieved at N/P ratios less than or equal to about 10.
63. The method of claim 61, wherein optimum cell transfection efficiency is achieved at N/P ratios between about 6 and 9.
- 15 64. The method of claim 50, wherein the administering is in vitro.
65. The method of claim 50, wherein the administering is in vivo.
- 20 66. The method of claim 65, wherein the complex is administered to a mammal.
67. The method of claim 65, wherein the complex is administered to a human.
68. The method of claim 60, wherein the administering comprises introduction of the
25 complex into the body of a mammal.
69. The method of claim 68, wherein the administering results in a prolonged expression of the therapeutic gene which extends more than 72 hours after introduction of the complex.
- 30 70. The method of claim 68, wherein the administering results in prolonged expression of the therapeutic gene which extends for eight days after introduction of the complex.

71. The method of claim 60, wherein introduction of the complex to the body of a mammal results in transfection of cells by the complex and expression of the therapeutic gene in organs located at a distance from a site at which the complex was introduced.

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72. The method of claim 71, wherein the therapeutic gene is expressed in a lymph node of the mammal.

73. The method of claim 50, wherein the complex has diameter of less than or equal to about 100 nm.

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74. The method of claim 50, wherein the complex has a diameter of between about 50 and 100 nm.

75. The method of claim 50, wherein the complex has a diameter of between about 50 and 70 nm.

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76. The method of claim 50, wherein the nucleic acid molecule comprises siRNA.

77. A method for manufacturing a medicament for use in delivery of a nucleic acid in vivo comprising:

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providing a nucleic acid molecule; and

combining the nucleic acid molecule with a hyperbranched dendron polymer selected from at least one of the group consisting of

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(a) a flexible hyperbranched dendron polymer comprising: a surface defined by the polymer, a polyethyleneimine core within the surface, a plurality of primary amine groups at the surface, and a plurality of secondary and tertiary amine groups positioned at the core.;

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(b) a hyperbranched dendron polymer having a randomly branched structure, a molecular weight of about 10 to 25 kD, and a ratio of secondary to tertiary amine groups of less than or equal to about 1.5 to 1.; and

- (c) hyperbranched dendron polymer made by a process comprising iterative attachment of ethyleneimine moieties to a branched polyethyleneimine core, wherein the process increases the amount of secondary and tertiary amines in the polymer while maintaining a plurality of primary amines on a surface of the polymer.